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EXAMINER
GABEL, GAILENE

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/548,883	WATKINS ET AL.	
	Examin r	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-22* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☒ Claim(s) *1-25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group 1, claims 1-22, with traverse, in Paper No. 8 is acknowledged and has been entered. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. Specifically, claim 1 recites "a) incubating said sample with a mixture of particles in a first suspension", "b)

recovering ... and incubating said recovered particles with a mixture of labeled binding members", c) recovering ... and detecting the amount of" but fails to distinctly define a functional relationship that exists between the four biological markers, if any, in the sample and the specific anti-thyroid antibodies coated on the particles as set forth in step a) and the labeled anti-thyroid antibodies or analogs thereof set forth in b), so as to effect a detection step. For example, does a binding interaction take place between each of the elements in each group; thereby forming complexes in the mixtures and wherein the presence of specific complexes is indicative of the presence of the biological marker.

Accordingly, it is unclear in step a) how each group in I), ii), iii), and iv) is distinguishable from each other by flow cytometry, i.e. size, shape, type of antibody immobilized thereto.

The preamble requires determining levels of "four biological markers indicative of thyroid disorders" but fails to distinctly and clearly define, or relate these four biological markers with "thyroid stimulating hormone, triiodothyronine, thyroxine, and anti-thyroid peroxidase recited in step c), lines 5-6.

Claim 1, step b) 2) is indefinite in reciting, "a labeled analog composition" because it is unclear what is encompassed by the term "composition" as recited in the claim.

Claim 1, step b) 3) is ambiguous in reciting, "either labeled anti-human IgG when particles of group (iv) are coated ... or labeled thyroid peroxidase when particles of

group (v) are coated ..." because the recitation of group (v) lacks antecedent support, i.e. there is no previous recitation of "group (v)".

Claim 1, step c) is indefinite and confusing. It is unclear what Applicant intends to encompass in reciting, "detecting the amount of label bound to said particles thus recovered" because it is unclear how the label "bound" to the particles. Also, it is unclear as to whether Applicant refers back to the recovered particles in b) or the recovered particles in c) in reciting, "thus recovered".

Claim 1, step c) is further indefinite in reciting, "correlating ... the amount of label thus detected to the group to which said label is bound, thereby simultaneously obtaining values individually representative of the levels of" because it appears to intend differential detection between each of the biological markers; however, there are no indications anywhere in the claim how this can be effected, i.e. the particles are recited as distinguishable which appears to be by virtue only of the specific thyroid antibody that is immobilized thereto, the labeled antibodies are recited as "labeled" by what appears to be the same label for each of the four biological markers, the binding interaction between each of the elements is not clearly defined and the resulting complexes not clearly set forth. For these reasons, it is unclear how differential detection of thyroid stimulating hormone, triiodothyronine, thyroxine, and anti-thyroid peroxidase is performed.

Claims 2-22 have improper antecedent basis problems in reciting, "A method in accordance with claim...".

Claim 3 is indefinite because it appears to intend differential detection between each of the four biological markers and including thyroglobulin; however, there are no indications anywhere in the claim or claim 1 from which it depends, how this can be effected, i.e. in claim 1, the particles are recited as distinguishable which appears to be by virtue only of the specific thyroid antibody that is immobilized thereto, the labeled antibodies are recited as "labeled" by what appears to be the same label for each of the four biological markers, the binding interaction between each of the elements is not clearly defined and the resulting complexes not clearly set forth. For these reasons, it is unclear how differential detection of thyroid stimulating hormone, triiodothyronine, thyroxine, anti-thyroid peroxidase, and anti-thyroglobulin is performed.

Claim 4 is vague and indefinite in reciting, "said labeled analog composition of b) 2) is a single species having immunological binding affinity to both anti-triiodothyronine and anti-thyroxine" because, it is unclear how differential detection between triiodothyronine and thyroxine is performed using anti-thyroid peroxidase and anti-thyroglobulin because it appears that the labeled analog binds both triiodothyronine and thyroxine.

It is unclear how differential detection of thyroid stimulating hormone, triiodothyronine, thyroxine, and anti-thyroid peroxidase is performed using a "common label" as recited in claim 11.

Claim 12 is ambiguous in reciting, "said particles incorporate dyes" because it is unclear how the dyes are incorporated into the thyroid antibodies of groups I) to iv by

the particles. It is further unclear how the distinct dyes and the labels recited in the instant claim are related and differentially detected by flow cytometry.

Claim 12 is indefinite because it is unclear how the label is bound to the particle.

Claim 20 is vague and indefinite in reciting, "two subgroups differing from each other by particle size such that one subgroup provides substantially greater sensitivity" because it is unclear as recited how the particle size relates to the level of sensitivity. See also claim 22.

Claim 20 is indefinite in reciting, "useful" because the term "useful" is a subjective term that lacks a comparative basis for defining its metes and bounds. See also claim 22.

Regarding claim 20, the phrase "than the other" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "than the other"), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d). See also claims 21 and 22

Claim 21 is vague and indefinite in reciting, "two subgroups differing from each other by coating density ... such that one subgroup provides substantially greater sensitivity" because it is unclear as recited how the coating density relates to the level of sensitivity. See also claim 22.

Claim 21 is indefinite in reciting, "useful" because the term "useful" is a subjective term that lacks a comparative basis for defining its metes and bounds. See also claim 22.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-2, 7-15, and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824).

Watkins et al. disclose a multiplex flow assay for analyzing a single patient sample to simultaneously determine biological markers indicative of thyroid function or disorders (see column 3, lines 6-26). According to Watkins et al., multiple combination assays can be performed on the single patient sample; thus combining competitive, sandwich, immunometric, and serological assays such as assays for thyroid stimulating hormone (TSH) and free thyroxine (T_4) or total T_4 (see column 9, lines 27-34).

Specifically, Watkins et al. disclose incubating the sample with a mixture of solid phase particles in a suspension having anti-TSH antibody coated thereto. Simultaneously or sequentially, the sample is recovered and further incubated with a second anti-TSH antibody that binds another epitope of TSH which is conjugated with a label, i.e. phycoerythrin (see column 8, lines 33-52). Watkins et al. disclose that the solid phase particles may be provided in different groups wherein each group has different antibodies immobilized thereto; i.e. these antibodies in each group are specific to the different immunoglobulin classes such as anti-IgM antibodies and anti-IgG antibodies (see column 10, lines 20-60). Watkins et al. specifically use solid magnetic particles as solid phase which are classifiable by flow cytometry into discrete groups according to distinguishable characteristics, differentiation parameters, and specific antibodies or antigens (assay reagents) which bind in a selective manner (see column 3, lines 6-27 and column 7, line 65 to column 8, line 6). Differentiation parameters include size, fluorescence labels, angle scatter, light emission, density, absorbance, and number of particles for each group (see columns 6-7). The solid particles comprise magnetically responsive materials wherein recovery of these materials after incubation is achieved by subjecting the suspensions to magnetic field to cause the particles to adhere to a reaction vessel wall (see column 3, lines 28-37 and column 8, lines 11-32). Each solid particle group has a fluorescein dye incorporated thereto at differing concentrations and the assay specific antibodies or antigens are labeled with phycoerythrin (see column 6, lines 40-52).

Watkins et al. differ from the instant invention in failing to disclose further assaying the patient sample for triiodothyronine (T_3) and human thyroid peroxidase (hTPO) as biological markers in determining thyroid disorder or function.

Dietzen discloses that a full understanding of thyroid function requires accurate assessment of the amounts of TSH, T_3, and T_4. Dietzen, therefore, provides a standard solution which contains specific amounts of TSH, T_3, and T_4 for use in simultaneous multiple thyroid related-analyte binding assays (see column 2, lines 56-67). The standard also contains serum bovine albumin as the binding protein or diluting agent for the standard (see column 5, lines 15-41). According to Dietzen, large glycoproteins such as TSH are measured by two-site sandwich immunoassay technology, i.e. using anti-TSH antibodies as capture and detection antibodies. Smaller molecules at smaller concentrations such as T_3 and T_4 are determined by competitive hapten immunoassay using anti-T_3 antibodies and anti-T_4 antibodies (see column 6).

Weckermann et al. disclose that human thyroid peroxidase (hTPO) is a glycosylated hemopoietin which is bound to thyroid membranes and performs an important function in the biosynthesis of thyroid hormones (see page 1, paragraph 2). The hTPO is identical to a microsomal antigen which is recognized as autoantigen of circulating anti-thyroid antibodies, i.e. anti-hTPO, (autoantibodies) which are detected in patients having autoimmune disease of the thyroid. These anti-thyroid antibodies, thus, play an important role as biological markers in assessing thyroid function or disorder (see page 2). Weckermann et al. disclose immobilizing monoclonal anti-hTPO antibodies into solid phase particles and labeling anti-hTPO antibodies for use as

binding partners in a sandwich assay for quantitative determination of hTPO. The first mAb is specific for a region of the hTPO that is involved in binding of autoantibodies against hTPO. Alternatively, Weckermann et al. disclose preparing standards comprising hTPO from human thyroid membranes which are purified by affinity chromatography for use in binding assay with anti-hTPO antibodies (see page 11, lines 27-30). Recombinant hTPO is also commercially available in a buffer solution (see page 12, lines 1-8).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Dietzen and Weckerman in assaying for T_3 and hTPO with the multiplex method for assaying TSH and T_4 utilizing groups of identifiable particles, i.e. beads, as taught by Watkins because Watkins specifically taught that his method allows for simultaneous multiple determination and differentiation of physiologically related analytes such as TSH, T_4, T_3, and hTPO which are all analytes that can provide individually and cumulatively, an assessment of thyroid function.

Watkins, Dietzen, and Weckermann have been discussed supra. Watkins, Dietzen, and Weckermann does not teach that hTPO can be coated to particles at a density of 0.3 ng/cm^2 to about 1.0 µg/cm^2 and at a density of 0.5 ng/cm^2 to about 50 ng/cm^2 in claims 18 and 19.

It is, however, maintained that parameters, i.e., density coating of 0.3 ng/cm^2 to about 1.0 µg/cm^2 and 0.5 ng/cm^2 to about 50 ng/cm^2 are all differentiation parameters comprising result effective variables which Watkins has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine

experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 18-19 are for any particular purpose or solve any stated problem and the prior art teaches that differentiation parameters often vary according to the reagent being used or sample being assayed, solutions and parameters utilized by Watkins appear to work equally as well. Therefore, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the method disclosed by the Watkins by normal optimization procedures.

5. Claims 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824).as applied to claims 1-2, 7-15, and 18-19 above, and further in view of Frengen (US 5,723,346).

Watkins, Dietzen, and Weckermann have been discussed supra. Watkins, Dietzen, and Weckermann differ from the claimed invention in failing to disclose use of

two subgroups differing in particle size and/or coating density so as to provide greater sensitivity for lower concentrations of TSH.

Frengen discloses a binary assay method capable of providing a wide dynamic range and a high degree of precision wherein two subgroups of particles differing from each other in particle size and coating density, i.e. diameter, composition, reactive surface groups, are used (see column 3, lines 47-55 and column 6). Specifically, Frengen discloses reacting a sample with a first binding partner having affinity for a biological marker, i.e. thyroid function marker, a labeled ligand having affinity for the marker, a second binding partner having affinity for the labeled ligand, wherein the first and the second binding partners are independently distinguishable and determinable particle forms and the marker concentrations obtained therefrom are determined using a standard curve (see column 3, lines 56-67).

One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the binary assay using two distinguishable particles taught by Frengen into the multiplex assay method as taught by Watkins because Frengen specifically taught that incorporating binary systems into sandwich assays such as the TSH assay of Watkins provides for a wider or broader dynamic range, particularly in high analyte concentrations wherein the dynamic range would, otherwise, be limited by a phenomenon called hook effect which is usually seen in increased amounts of analyte .

6. Claims 3 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824).as applied to claims 1-2, 7-15, and 18-19 above, and further in view of Smith et al. (US 4,332,784).

Watkins et al., Dietzen, and Weckermann have been discussed supra. Watkins et al., Dietzen, and Weckermann differ from the instant invention in failing to disclose further assaying the patient sample for anti-thyroglobulins as biological markers in determining thyroid disorder or function.

Smith et al. disclose dual isotope assays for assessing thyroid function or disorder. Smith et al. disclose carrying out an assay for two of TSH, T_3, T_4, and thyroxine binding globulins or thyroglobulin (TBG) which play an important role as biological markers in assessing thyroid function or disorder (see Abstract). Smith et al. disclose an assay for determining T_3 and T_4 using anti-T_4 and anti-T_3 antibodies as immunological binding partners in Example 4, TSH and T_4 using anti-T_4 antibodies and anti-TSH antibodies as immunological binding partners in Example 5, and T_4 and TBG using anti- T_4 and anti-TBG antibodies as immunological binding partners to react and bind T_4 and TBG in Example 6 (see columns 7-8). Smith et al. also use human serum with calibrated T_4 and TBG levels as standards. Smith et al. disclose adding a solution containing 20% w/v polyethylene glycol (PEG) as a solute in the suspension with the binding components to terminate reaction and precipitate bound components in the assay reaction (see column 7, lines 1-6).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Smith in assaying for anti-TBG with the multiplex method for assaying TSH and T_4 utilizing groups of identifiable particles, i.e. beads, as taught by Watkins and modified by Dietzen and Weckerman by additionally assaying for T_3 and hTPO, because Watkins specifically taught that his method allows for simultaneous multiple determination and differentiation of physiologically related analytes such as TSH, T_4, T_3, hTPO, and TBG which are all analytes that can provide individually and cumulatively, an assessment of thyroid function.

Watkins, Dietzen, Weckermann, and Smith have been discussed supra. Watkins, Dietzen, Weckermann, and Smith do not teach concentrations of 0.5% to about 4.0% by weight of PEG in claim 16 and 2.0% to about 3.0% by weight of PEG in claim 17.

It is, however, maintained that parameters, i.e., solute concentrations in assay reagents and buffers, comprise result effective variables which Smith has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within

the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 16 and 17 are for any particular purpose or solve any stated problem and Smith teaches that concentration of PEG often vary according to reagent usage, concentration parameters of PEG utilized by Smith appear to work equally as well. Therefore, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the method disclosed by the Smith by normal optimization procedures.

7. Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824).as applied to claims 1-2, 7-15, and 18-19 above, and further in view of Evans et al. (US 5,071,773).

Evans et al. disclose that specific analogs of thyroid hormones have characteristic competition patterns for T_3 binding to the native thyroid hormone receptor. Evans et al. demonstrate competition binding of T_3 which is achieved with 3,5',3'-triiodo-L-thyronine.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute 3,5-triiodo-L-thyronine as taught by Evans for the anti-triiodothyronine and anti-thyroxine in the method of Watkins as modified by Dietzen and Weckermann, for use in a competition binding assay, because Evans specifically taught its application with competitive binding methods and Watkins and Dietzen are generic

with the type of immunological binding partners used for T_3 and T_4 in competitive assays.

Allowable Subject Matter

8. Claim 6 would be allowable if rewritten to overcome the rejection under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. Prior art of record fails to teach or fairly suggest using labeled N-acetyl-3-iodo-L-tyrosine as a single species having immunological binding affinity for both T_3 and T_4 in a competitive binding assay to assess thyroid function alongside with TSH and hTPO.

Remarks

9. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Chandler et al. (US 5,981,180) disclose multiplex analysis of clinical specimens by using appropriately labeled beadsets with specific antigens or antibodies immobilized thereto to simultaneously detect various different biomolecules in flow cytometry.

Ward (US 4,032,626) discloses that a diagnosis of the dysfunction of the thyroid gland and related organs and systems is facilitated by rapid and accurate assay of TSH, T_3, T_4, and globulins such as thyroxine binding globulins or thyroglobulins (TBG); thus, anti-thyroglobulins play an important role as biological markers in assessing thyroid function or disorder (see column 1, lines 11-21). Ward discloses an assay for

determining TBG using anti-TBG antibodies immobilized into solid phase particles and radiolabeled for detection (see column 2, line 44 to column 3, line 8). Ward prepares a standard curve of several TBG antigen concentrations for use in direct measurement of TBG concentrations.

Chang et al. (US 4,824,777) disclose a method of determining thyroxine uptake (see Summary).

Bergmann et al. (US 5,639,670) disclose a method of determining thyroid hormone in free form and in a form bound to physiological binding proteins.

Renzoni et al. (US 5,346,670) disclose attaching a separate fluorescent label for each of T_3, T_4 and TSH in performing simultaneous thyroid panel test (see column 17, lines 30-37).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
February 20, 2002

LONG V. LE
SUPERVISORY PATENT EXAMINER
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02/24/02